Remarks

Claims 48, 52, 54, 61 and 69-71 are pending in this application. Claims 50, 53, 55-60 and 63-68 are canceled without prejudice to Applicants' right to pursue the subject matter recited by them in one or more divisional, continuation, or continuation-in-part applications.

Claim 48 is amended to recite, in part, a pharmaceutical composition for the treatment of allergic rhinitis or urticaria comprising about 0.1 mg to 5 mg of descarboethoxyloratadine ("DCL"). The support for the amendment can be found, for example, on page 14, lines 11-17 of the specification. Claim 54 is made dependent from claim 48. Claim 61 is amended to remove its dependency from canceled claims.

New claim 69 is added to recite the specific amount of 5 mg of DCL. Claims 70 and 71 are added to recite a composition to be administered in a single daily dose and a composition in the form of a tablet or a capsule, respectively. The support for these claims can be found, for example, on page 14, lines 6-15 and page 16, lines 10-14 of the specification, respectively. No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 112 Should Be Withdrawn

On page 2 of the Office Action, claim 65 is rejected because the term "elixir" is allegedly indefinite. Although Applicants respectfully disagree with the Examiner's contention, this rejection is moot in view of the cancellation of claim 65. Consequently, Applicants respectfully request that the rejection of claim 65 under 35 U.S.C. § 112 be withdrawn.

B. The Rejection Under 35 U.S.C. § 102 Should Be Withdrawn

On pages 2-3 of the Office Action, claims 48, 52 and 54 are rejected as allegedly anticipated by U.S. Patent No. 4,659,716 to Villani *et al.* ("Villani") for the reasons stated in the Office Action. Applicants respectfully traverse this rejection.

Although Applicants respectfully disagree with the Examiner's contention, claim 48 is amended solely to expedite the prosecution of this application. Claim 48 recites, in part, a pharmaceutical composition for the treatment of allergic rhinitis or urticaria which comprises about 0.1 mg to 5 mg of DCL. Villani does not disclose a pharmaceutical composition for the treatment of allergic rhinitis or urticaria, much less a pharmaceutical

composition for the treatment of allergic rhinitis or urticaria comprising about 0.1 mg to 5 mg of DCL. In other words, the specific dose of the specific compound in a specific pharmaceutical composition is not disclosed by Villani, and thus Villani cannot anticipate the claimed invention. Therefore, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102 be withdrawn.

C. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 3 to 6 of the Office Action, claims 48, 52 and 54 are rejected as allegedly obvious over Villani.[1] Applicants respectfully traverse this rejection.

The Patent Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103. *In re Deuel*, 51 F.3d 1552, 1557 (Fed. Cir. 1995); *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). To establish a *prima facie* case of obviousness, the Patent Office must first show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, it must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the Patent Office must show that the prior art teaches or suggests all the claim limitations. *See In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *Manual of Patent Examining Procedure*, § 2143.

First, Applicants respectfully submit that Villani does not disclose or suggest all of the limitations of the pending claims. For example, Villani does not disclose or suggest a pharmaceutical composition for the treatment of allergic rhinitis or urticaria. Villani also does not disclose or suggest a pharmaceutical composition comprising about 0.1 mg to 5 mg of DCL. This is because only amount range provided in Villani for the compounds it discloses is from 1 mg to 1000 mg. Villani, col. 8, lines 42-44. For this reason alone, Applicants respectfully submit that the rejection be withdrawn.

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[1] Applicants note that Berkow *et al.*, *Merck Manual of Diagnosis and Therapy*, 16th Ed. (Merck and Co., Rahway, NJ), pp. 324-7 and 3245-7 (1992) ("Berkow") and Gennaro *et al.*, *Remington's Pharmaceutical Sciences*, 18th Ed. (Philadelphia College of Pharmacy and Science), pp. 1097-1130 (1990) ("Gennaro") are also cited in connection with the rejection under 35 U.S.C. § 103. As Berkow and Gennaro are cited to show the second therapeutic agents, *i.e.*, a decongestant and an NSAID, but the pending claims no longer recite those agents, the rejection is addressed in connection with Villani only.

Second, Applicants respectfully submit that Villani would not have motivated those of ordinary skill in the art to use DCL in a pharmaceutical composition for the treatment of allergic rhinitis. Indeed, not only would Villani not have provided motivation to make a composition of the specific compound DCL at all, it also would not have motivated those of ordinary skill in the art to make a composition comprising from about 0.1 mg to 5 mg of DCL.

In fact, while disclosing that the compounds it discloses may be used in an amount of from 1 to 1000 mg, Villani provides several exemplary compositions which contain the purportedly active compound in the range of several hundred milligrams. The following summarizes the amount of "active compound" disclosed in connection with the compositions in Villani: 1) Example A: 100 or 500 mg; 2) Example B: 100 or 500 mg; 3) Example C: 100 or 500 mg; 4) Example D: 100 mg; 5) Example E: 200 mg; 6) Example F: 200 mg; 7) Example G: 200 mg; 8) Example H: 200 mg; and 9) Example I: 100 mg. *See* Villani, cols. 22-24.

Therefore, by disclosing the wide range of amount, *i.e.*, 1 to 1000 mg, and providing only the compositions that contain several hundred milligrams of "active compound," Villani effectively teaches those of ordinary skill in the art away from the low doses of DCL, which the pending claims recite.

In addition, significantly, those of ordinary skill in the art would have been generally discouraged from using DCL for the treatment of allergic rhinitis or urticaria. This is because DCL was, at the time of the claimed invention, known to be a member of a group of molecules that caused serious adverse effects. *See*, Storms Declaration,[2] ¶ 12-15. Similarly, since DCL is a metabolite of loratadine, there were concerns that DCL could be associated with tumor growth or personality changes. *See Id.*, ¶ 17. This knowledge would certainly have cut against any suggestion or motivation, if there was any, by Villani to make and try a pharmaceutical composition of DCL, much less a pharmaceutical composition containing the specific amount of DCL, to treat allergic rhinitis or urticaria. Applicants refer to ¶ 12-17 of Storms Declaration. For this reason alone, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

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[2] Storms Declaration was submitted to the European Patent Office ("EPO") in connection with a related application in Europe. For the Examiner's convenience, Applicants point out that the EPO has decided to grant claims in that application.

Third, Villani also fails to provide a reasonable expectation of successfully making and using the claimed invention. Although Villani purportedly discloses DCL's efficacy in reducing histamine-induced paw edema in rats, such a crude assay does not even provide confirmation that the compounds tested would be useful against allergic disorders. This is because, while agents that selectively prevent histamine binding to H_1 histamine receptor ("H_1 antagonists") may be used for the treatment of allergic disorders, agents that prevent histamine binding to other histamine receptors ("H_2 or H_3 antagonists") may not. *See* Storms Declaration, ¶ 6-7. Yet, certain H_2 and H_3 antagonists were known to reduce histamine-induced paw edema in rodents. *Id.*, ¶ 8-9. Therefore, the disclosure of Villani that DCL reportedly reduces the histamine-induced paw edema in rats would not have suggested to those of ordinary skill in the art that DCL can be used for the treatment of allergic disorders, and thus, those of ordinary skill in the art would not have had a reasonable expectation of successfully making and using the claimed invention. For this additional reason, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

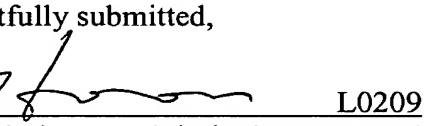
Conclusion

For at least the foregoing reasons, Applicants respectfully submit all of the pending claims are allowable, and thus respectfully request the allowance thereof.

No fee is believed due for this submission. Should any additional fees be required for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

Date August 12, 2005



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